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EXAMINER	
STRZELECKA, TERESA E	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 03/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/642,068	STUELPNAGEL ET AL.	
	Examiner	Art Unit	
	Teresa E. Strzelecka	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-10,27-31 and 33-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-10,27-31 and 33-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 22, 2005 and December 19, 2005 has been entered.

2. Claims 2-10, 27-31 and 33-37 were previously pending. Applicants did not amend any claims. Claims 2-10, 27-31 and 33-37 are pending and will be examined.

3. All of the previously presented rejections are maintained for reasons given in the "response to Arguments" below. New grounds for rejection are presented.

Response to Arguments

4. Applicant's arguments filed April 22, 2005 and December 19, 2005 have been fully considered but they are not persuasive.

A) Regarding the rejection of claims 2-10, 27-31 and 33-37 under 35 U.S.C. 103(a) over Holmes and Beattie, all of the arguments seem to be centered on the term "pool of oligonucleotides" and the showing of rationale in Holmes "for releasing a mixture of oligonucleotides from an array precisely assembled... just to thereafter combine them into a pool of mixed oligonucleotide species".

A) Regarding the term "pool of oligonucleotides", Applicants arguments can be summarized as a conclusion that neither Holmes nor Beattie et al. teach or suggest a step of generating a pool of oligonucleotides. However, as explained in several of the previous office actions, Applicants' definition of a pool encompasses any two oligonucleotides. Therefore, if, as Holmes teaches,

synthesis of oligonucleotides is performed on discrete areas containing beads and release of the oligonucleotides from the beads (col. 6, lines 34-37), as well as synthesis of multiple polymers on multitude of beads performed in any one of the containers (col. 9, lines 40-67; col. 10, lines 1-14), then release of the oligonucleotides from the beads will cause at least two oligonucleotides to be freed from the beads, generating a pool. Further, the following paragraph from Holmes (col. 12, lines 6-16, cited in previous office actions), states the following:

"In another aspect, the present invention provides novel compounds which are useful as photochemically cleavable linking groups. Linking groups which are photochemically cleavable are useful in several applications. In one application, these linking groups can be used for the photoinduced release of oligomers or small ligand molecules from a surface for characterization purposes following a bioassay. In another application, such linking groups are useful for the mild cleavage of oligomers from a surface after various side chain protecting groups are removed. The oligomers can then be used in subsequent bioassays."

Therefore, Holmes specifically teaches generation of oligonucleotide pools.

Now on to Beattie et al., who, in column 8, lines 31-48 (cited previously) state the following:

"In another aspect of the present invention, there is provided an improved method of preparing oligonucleotide arrays for use in hybridization analyses, comprising the steps of: chemically synthesizing a desired set of oligonucleotide probes using 3'-amino-C3 controlled pore glass support material to produce completed desired oligonucleotides; cleaving said completed desired oligonucleotides from said support material in concentrated ammonium hydroxide to yield oligonucleotides bearing aminopropanol groups at their 3'-termini; cleaning a glass or silicon dioxide surface with organic solvents and drying at elevated temperature; applying a quantity of

oligonucleotides bearing aminopropanol groups at their 3'-termini in aqueous solution to said surface of said clean, dry glass or silicon dioxide; allowing covalent bonding of said oligonucleotides bearing aminopropanol groups at their 3'-termini to said surface through terminal aminopropanol functions; and removing unbound oligonucleotides from the surface by washing with water."

Therefore, Beattie et al. also specifically teach creating oligonucleotide pools by cleaving multiple oligonucleotides from their supports before attaching them on an array.

B) Regarding the rationale in Holmes for releasing the oligonucleotides, Holmes does not teach them being assembled "in a precise array", as interpreted by Applicant. The oligonucleotides of Holmes are contained in batches of beads in a single or multiple containers (col. 9, lines 30-67; col. 10, lines 1-15). Again, the rationale of Holmes for releasing the oligomers is that they are used in subsequent bioassays (col. 6, lines 13-16).

In conclusion, both Holmes and Beattie et al. provide specific teaching of creating of pools of oligonucleotides according to Applicant's definition, and a rationale for cleaving the oliguncleotides from their supports.

The rejection is maintained.

Claim interpretation

5. The following interpretation of claim limitations is used to evaluate correspondence between the current claims and prior art:

A) Applicants defined the term "pool" in the following way (page 8, last paragraph):

"By "pool" is meant a plurality or more than one solution-phase oligonucleotide."

B) The term " first and second linkers" is interpreted as linkers which may be the same, as there is no requirement that they have to be different.

C) The term "chip" in claim 29 is interpreted as any substrate (it is used interchangeably with "substrate" in the claim. Applicants' definition on page 16, fourth paragraph: "... By "chip" or biochip" herein is meant a planar substrate to which nucleic acids are directly or indirectly attached."

D) Applicants did not define the term "array" therefore any arrangement of oligonucleotides bound to a solid support is considered to be an array.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 2, 5-9, 27-31 and 33-37 are rejected under 35 U.S.C. 102(e) as being anticipated by Kuimelis et al. (U.S. patent No. 6,537,749 B2) as evidenced by Lashkari et al. (PNAS USA, vol. 92, pp. 7912-7915, 1995).

Since claim 29 is specie of claims 27 and 30 and claims 33 and 35 are restated versions of claim 27, and claims 28 and 34 differ from claim 29 by the support being beads, only steps of claim 29 are discussed explicitly.

Regarding claims 27-30 and 33-35, Kuimelis et al. teach multiplex detection of target nucleic acids, the method comprising:

a) providing an array comprising a substrate and a population of oligonucleotides, said population comprising at least first and second subpopulations, wherein said first subpopulation comprises at least a first oligonucleotide and, wherein said second subpopulation comprises at least

a second oligonucleotide, wherein said first oligonucleotide is different from said second oligonucleotide and, wherein said first and second oligonucleotides are of known sequence, said first and second oligonucleotides being immobilized directly to said substrate through first and second cleavable linkers, respectively (Kuimelis et al. teach synthesis of capture probes (= oligonucleotides) on a solid support and attachment of the oligonucleotides to the solid support by cleavable linkers, therefore they teach an array of oligonucleotides (col. 10, lines 6-25; col. 11, lines 62-67; col. 12, lines 1-52; col. 15, lines 16-67). Kuimelis et al. teach capture probes of known sequence (col. 12, lines 1-20; col. 15, lines 39-48).);

b) cleaving said first and second linkers, thereby releasing said first and second subpopulations from said substrate thereby generating a pool of oligonucleotides comprising said first and second oligonucleotides (Kuimelis et al. teach cleaving the first and second linkers and releasing the oligonucleotides from the support, therefore they inherently teach creating the pools of oligonucleotides, as defined by Applicants (col. 10, lines 20-25; col. 12, lines 45-49; col. 15, lines 64-67).); and

c) contacting said first and second oligonucleotides with a composition comprising at least a first and second target nucleic acid, whereby said first and second target nucleic acids hybridize with said first and second oligonucleotides whereby said target nucleic acids are detected (Kuimelis et al. teach attachment of capture probes to another solid support and hybridization of at least two target nucleic acids to detect them (col. 1, lines 37-49; col. 2, lines 15-22; col. 6, lines 34-46; col. 13, lines 52-67; col. 14, lines 1-19; col. 16, lines 59-67; col. 17, lines 1-19).).

Regarding claims 28 and 34, Kuimelis et al. do not specifically teach the support being beads, however, they teach that the oligonucleotides were synthesized in an automatic DNA synthesizer on controlled-pore glass (CPG) supports (col. 10, lines 7-11). Lashkari et al. teach

DNA synthesis in an automated DNA synthesizer (Abstract), where the CPG support is a collection of beads (page 7913, fourth paragraph; Fig. 4). Therefore, by teaching automated DNA synthesizer with CPG support Kuimelis et al. inherently teach beads as a support.

Regarding claim 2, Kuimelis et al. teach capture probes of known sequence (col. 12, lines 1-20; col. 15, lines 39-48).

Regarding claims 5, 8 and 31, Kuimelis et al. teach covalent attachment of the probes to the synthesis substrate via hexaethylene oxide or amino and hydroxyl groups (col. 10, lines 6-25).

Regarding claims 6 and 9, Kuimelis et al. teach synthesis of the oligonucleotides on the substrate (col. 10, lines 6-25; col. 12, lines 21-40; col. 15, lines 49-67).

Regarding claims 7 and 8, Kuimelis et al. teach synthesis of different oligonucleotides on a solid support (col. 10, lines 6-25; col. 12, lines 21-40; col. 15, lines 49-67). As evidenced by Lashkai et al., the support consists of beads (page 7913, fourth paragraph; Fig. 4), therefore by teaching synthesizing DNA in an automated synthesizer Kuimelis et al. inherently teach a discrete sites to which the oligonucleotides are linked.

Regarding claims 36 and 37, Kuimelis et al. teach glass supports (col. 10, lines 9-11), therefore, since Applicants did not define the term chip, Kuimelis et al. teach a chip.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 2-10, 27-31 and 33-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Holmes (U.S. Patent No. 5,679,773; cited in the previous office action) and Beattie (U.S. Patent No. 6,156,502; cited in the previous office action).

A) Since claims 28 and 29 are species of claims 27 and 30, the newly added claims 33 and 35 are restated versions of claim 27 and the newly added claim 34 is a restated version of claim 29, only steps of claims 28 and 29 are discussed explicitly.

Regarding claims 27-30 and 33-35, Holmes teaches a method of synthesis and release of nucleic acids, the method comprising:

a) providing a substrate and a population of oligonucleotides, said population comprising at least first and second different oligonucleotides, respectively, said first and second oligonucleotides being immobilized to first and second beads, respectively, through first and second cleavable linkers, respectively, said first and second beads being distributed on said substrate (Holmes teaches providing a substrate and compounds, such as oligonucleotides, synthesized on solid supports (= substrate), which may contain wells. Compounds are synthesized on beads distributed on the surface of the support (Abstract; col. 5, lines 64-67; col. 6, lines 26-37; col. 19, lines 58-67; col. 20, lines 1-7; col. 22, lines 11-16). Holmes teaches preparation of high-density arrays of diverse oligonucleotides (col. 2, lines 1-7; col. 10, lines 15-25), therefore Holmes teaches at least first and second oligonucleotides.);

b) cleaving said first and second linkers, thereby releasing said first and second subpopulations from said first and second beads, thereby generating a pool of oligonucleotides comprising said first and second oligonucleotides (Holmes teaches cleaving the oligonucleotide probes from the support (col. 6, lines 36, 37; col. 12, lines 6-16). Since Holmes teaches multiple

diverse oligonucleotides, cleavage generates a pool of oligonucleotides comprising first and second different oligonucleotides, anticipating this limitation.) ; and

c) contacting said first and second oligonucleotides with a composition comprising at least a first and second target nucleic acid, whereby said first and second target nucleic acids hybridize with said first and second oligonucleotides whereby said target nucleic acids are detected (Holmes teaches contacting the oligonucleotide array with a sample or using released oligomers in bioassays (col. 10, lines 18-21; col. 12, lines 15, 16). Holmes teaches using arrays for sequencing by hybridization (col. 1, lines 61-67).)

Regarding claim 2, Holmes teaches nucleic acids which are synthesized with DNA or RNA binding sequences which act as "receptors" for other nucleic acid sequences (col. 5, lines 64-66). Holmes does not specifically teach oligonucleotides with known sequences, but since they are synthesized to bind a specific sequence, their sequences must be known. Thus Holmes anticipates limitation of claim 2.

Regarding claim 3, Holmes teaches attaching labels to compounds synthesized on a substrate (col. 20, lines 33-67) and labeled beads attached to oligonucleotides (col. 10, lines 6-14).

Regarding claim 4, Holmes teaches labeled beads attached to oligonucleotides, where the beads are unique to each oligonucleotide or probe (col. 10, lines 6-14), anticipating the limitation of first and second oligonucleotides having different labels.

Regarding claims 5 and 31, Holmes teaches oligomers (e.g. oligonucleotides) attached to the solid support by covalent linkers, which are photochemically or chemically cleavable (col. 11, lines 23-67; col. 12, lines 6-16; col. 20, lines 7-32).

Regarding claims 6 and 9, Holmes teaches synthesis of oligonucleotides on a substrate (col. 6, lines 26-37; col. 22, lines 11-16).

Regarding claim 7, Holmes teaches substrate comprising discrete sites, such as wells, trenches, etc. (col. 6, lines 27-32).

Regarding claim 8, Holmes teaches beads distributed on a substrate and synthesis of oligomers on the beads (col. 6, lines 34-37; col. 9, lines 30-67; col. 10, lines 1-5).

Regarding claim 10, Holmes teaches synthesis of compounds by photolitography (col. 7, lines 23-40; col. 18, lines 1-67).

Regarding claim 36, Holmes teaches glass or silicon oxide as solid supports (col. 15, lines 43, 44) and a variety of other materials (col. 19, lines 58-67; col. 20, lines 1-7).

Regarding claim 37, Holmes teaches a flat rigid or semi-rigid substrate (col. 6, lines 26-28) and attachment of oligonucleotides to the surface (col. 19, lines 35-48; col. 5, lines 64-67), therefore, according to Applicants' definition, Holmes teaches a chip.

B) Holmes teaches oligonucleotide arrays, sequencing by hybridization and using cleaved oligonucleotides in bioassays, but does not specifically teach contacting the oligonucleotides with target nucleic acids.

C) Beattie teaches a method of oligonucleotide fingerprinting (ASOF), in which oligonucleotides cleaved from a solid support are contacted with a sample comprising target nucleic acids (Fig. 6; col. 8, lines 30-39; col. 12, lines 57-64). The target nucleic acids are contained in genomic DNA (col. 3, lines 14-27) or total RNA (col. 4, lines 14-16).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used the assay of Beattie to use oligonucleotides cleaved from solid support of Holmes. The motivation to do so, provided by Beattie, would have been that the ASOF assay was used in polymorphic marker analysis, species identification and transcriptional profiling without the need for electrophoresis (Abstract).

10. No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E. Strzelecka whose telephone number is (571) 272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

TERESA STRZELECKA
PATENT EXAMINER

3/5/06